

Remarks as Prepared For Delivery
Harvard Medical School Health Care Policy Seidman Lecture
"Manhattan Project for the 21st Century"

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I am a physician and a surgeon who by accident of fate finds himself in the halls of power at a time of dangers for his country and the world, the most compelling of which are exactly those a physician is trained to recognize and fight. To me it seems no more natural to be a United States senator, and in my case the majority leader of the Senate, than it did to Harry Truman, who spent so many hard and unambitious years as a farmer and then found himself in such a place and at such a time as he did. And, like him, as someone who comes from the outside, and for whom the perquisites of power appear strange and irrelevant, I ask myself what my purpose is as a public servant, what my obligations are, and what high precedents I should follow.

Also like Truman, I have never forgotten who I am, nor from whence I come, so I know my purpose, I know my duty and obligations, and I know the precedents to honor. Just as a surgeon must follow an objective course and a general must look at war with a cold and steady eye, a statesman must operate as if the world were free of emotion. And yet, to rise properly to the occasion, the surgeon must have the deepest compassion for his patient, the general must have the heart of an infantryman, and the statesman must know at every moment that the cost of his decisions is borne, often painfully, by the sovereign population he serves – all as if the world were nothing *but* emotion. The difficulty in this is what Churchill called the "continual stress of soul," the rack upon which the adherents of these professions, if they meet their obligations well, will of necessity be broken.

In balancing objectivity with emotion, the practical with the moral, the smooth operation of power with its homely and human effects, one is driven to consider first things and elemental purposes, and this consideration makes clear that the guiding star of statesmanship must be the fact of human mortality, and the first purpose of a public official a simple watch upon the walls. We are charged above all with assuring the survival of the nation and protecting the lives of those whom we serve and who have put us in our place, entrusting us with this gravest of responsibilities.

Whether leading a small nomadic band, captaining a ship, or at the head of a huge industrial nation, the task is the same. It is not merely that which can be accomplished with sword and shield, but, rather, the exercise of courage, sacrifice, and judgment, in the preservation of the life of a nation in its people as families and individuals. And as if by design, this task becomes in its execution a principle that unites the powerless and powerful in an unimpeachable equality.

In times of peace and prosperity, we sometimes forget that we are mortal, and the forgetfulness then can rule beyond its natural life even in the face of war and pestilence, when by all accounts the star of mortality shines in air cleared of the luminous distractions of peace.

It is human nature to look away from danger, to hope for the best, and pray that disaster will not arrive on our watch. But we will not be able to look away from what could be coming soon – a front of unchecked and virulent epidemics, the potential of which should rise above your every other concern. For what the world could soon face it did not see even in the great wars of the last century. And not only are we under prepared for these epidemics, we have not taken sufficient note of the fact that though individually each might be devastating, they are susceptible of either purposeful or accidental combination, in which case they could be devastating almost beyond imagination.

The history of pathogens advances in parallel with and is no more static than our own, with which it is always intertwined, even if at times invisibly. Sometimes it rushes forward with great speed and breathtaking evolutionary vigor, and sometimes it rests in slow backwaters. In 1967, the U.S. Surgeon General declared that we were within site of winning the war on infectious diseases. But that war was never won, not even in our most wishful thinking. Today more than a quarter of all deaths – fifteen million each year – are due to infectious diseases. Three million children die every year of malaria and diarrheal diseases alone, one child every ten seconds. As sobering as this may be, we have been nonetheless in a quiescent stage of the mutability of pathogens, a crawl from which they are now poised to break out. When viral diseases evolve normally – such as in the typical course of the human influenza virus undergoing small changes in its antigenicity and killing an average of 500,000 people annually throughout the world – it is called an *antigenic drift*. When they emerge with the immense power derivative of a jump from animal to human hosts followed by mutation and/or recombination with a human virus, as in the influenza pandemic of 1918 - 1919, in which 500 million people were infected and 50 million died, including half a million in the United States, it is called an antigenic *shift*.

To have believed with the Surgeon General forty years ago that the great advances of biological science were capable of permanently suppressing infectious disease was to have been unaware that these triumphs were appropriate only to one phase in the life of a continually evolving enemy whose natural rate of evolution and adaptation is far greater than our own. Shifts are the result of random, fortuitous, and unavoidable changes. Human population increase, concentration, and spread, intensification of animal husbandry, and greater wealth in developing countries bring animals both wild and domestic into closer contact with ever larger numbers of people. War, economic catastrophe, and natural disasters subdue active measures of public health. The unprecedented overuse of antibiotic medicines and products builds unprecedented resistance. Travel, trade, and climate change bring into contact disparate types and strains of disease. And as a consequence of all this, microbes evolve, mutate, and find new lives in new hosts, in new nations, on new continents.

The annual toll of infectious diseases worldwide – including four million from respiratory infections, three million from HIV/AIDS, and two million from waterborne diseases such as cholera – is a continuing and intolerable catastrophe that, while sparing no class, strikes hardest at the weak, the impoverished, and the young. But this is just a beginning, in that the evidence

suggests that we could be at the threshold of a major shift in the antigenicity of not merely one but several categories of pathogens, for rarely if ever have we observed among them such variety, richness, opportunities for combination, and alacrity to combine and mutate. HIV, variant Creutzfeldt-Jakob disease (mad cow), avian influenzas such as H5N1, and SARS are merely the lightning that however silent and distant gives rise to an approaching storm – a storm for which we are unprepared. But how can that be? How can the richest country in the world, with its great institutions, experts, and learned commissions, have failed to make every preparation – when preparation is all we need to fend off epidemics with the potential of killing hundreds, thousands, millions, and, yes, worldwide, tens of millions of people?

To see what might lie on the horizon one need only look to the relatively recent past. I have a photograph of an emergency hospital in Kansas during the 1918 influenza pandemic. People lie miserably on cots in an enormous barn-like room with beams of sunlight streaming through high windows. It seems more crowded than the main floor of Grand Central Station at five o'clock on a weekday. In this one room several hundred people are in the throes of distress. Think of two thousand such rooms filled with a crush of men, women, and children -- five hundred thousand in all – and imagine that the shafts of sunlight that illuminate them for us almost a century later are the last light they will ever see. Then bury them. That is what happened.

How would a nation so greatly moved and touched by the three thousand dead of September 11th react to half a million dead? In 1918 - 1919 the mortality rate was between 2.5 and 5 percent, which seems merciful in comparison to the 55 percent mortality rate of the current Avian flu. In just 18 months, this Avian flu has killed or forced the culling of more than 100 million animals. And now that it has jumped from birds to infect humans in 10 Asian nations, how many human lives will it or another virus like it take? How, then, would a nation greatly moved and touched by three thousand dead, react to five or fifty million dead?

How would we react to the devastation caused by a virus or bacteria unleashed not by nature, but intentionally by man? During the Cold War, the Soviet Union, which stockpiled 5,000 tons annually of biowarfare-engineered anthrax resistant to 16 antibiotics, also produced three tons of weaponized smallpox virus, just as the monumental effort to immunize the world's children came to a successful close. As a result of conditions prevalent during the dissolution of the USSR, it is impossible to rule out that quantities of this or other deliberately manufactured pathogens such as anthrax, pneumonic plague, tularemia, botulinum toxin and others may find or may have found their ways into the possession of terrorists such as bin Laden and A-Zarqawi. Although the United States now has enough smallpox vaccine for the entire population, it has neither the means of distribution nor the immunized personnel to administer it in a generalized outbreak nor the certainty that the vaccine would be relevant to a specific weaponized strain of the virus. Ring vaccination would be useless if smallpox were intentionally released at many sites simultaneously. Hospitals and our long neglected public health infrastructure would be quickly overwhelmed.

In such a circumstance, panic, suffering, and the spread of the disease would intensify as – because people were dead, sick, or afraid – the economy would become crippled, electrical power would flicker out, and food and medical supplies would fail to move. Over months or

perhaps years, millions might perish, with whole families dying and no one to memorialize them. Almost without doubt, the epidemic would spread to the rest of the world, for in biological warfare an attack upon one country is an attack upon all. Then we would find ourselves more than willing to return to even the most difficult times of the last century. Is such a scenario possible? Well, it is not impossible. Humanity has not moved beyond this kind of scenario. Of late it has moved unnecessarily toward it.

Any number of known and unknown viruses for which at present there is neither immunization nor cure are at this moment cooking in Asia and Africa, where they arise in hotbeds of densely intermingled human and animal populations. We are in unexplored territory. Economic and environmental changes in Asia have forced wilderness-deprived waterfowl to alight to feed amid farm animals in newly dense populations due to recently acquired wealth and dietary expectations, in a culture in which live poultry is brought to market. The reassortment of viral DNA as a result of this mingling is so frenzied that it is only a matter of time until the emergence of a virus unequaled in transmissibility and virulence. The epidemiological calculus of flu is notoriously volatile due to the unknowns of rapid reassortment. We do know now, however, that the incidence of H5N1 has been underestimated in China and North Korea and elsewhere, and that we are woefully under prepared even for a virus that we can foresee, much less for one that we cannot.

No such viruses have yet reached critical mass or leapt from the channels imposed by their inherent limitations, environmental obstacles, and deliberate actions to contain them. But who is to say they cannot? Right now, in Angola, an outbreak of Marburg Hemorrhagic Fever has already infected 399 people of which 335 have been killed. As a medical missionary, I have been on the ground in Kenya after an outbreak of Rift Valley Fever. As majority leader, I was in China to study the SARS outbreak at its height and the government's confused, deceptive and inadequate response. As an American doctor, I have personally treated patients in Sudan and Tanzania and other African countries and seen a determined epidemic -- HIV/AIDS -- kill millions and hollow out entire societies. With the evidence I have seen, the patterns of history, and new facts such as rapid, voluminous, and essential travel and trade; the decline of staffed hospital beds; and a now heavily urbanized and suburbanized American population dependent as never before upon easily disrupted networks of services and supply, lead me to believe that such viruses could result in the immensely high death tolls to which I have alluded.

For the virus that is currently the greatest threat, the Avian flu, a vaccine would not become available, at best, until six to nine months after the outbreak of a pandemic. Even then that vaccine would not be available en masse. And even then we do not know if that vaccine would work. It is still experimental. So, in essence, we have no vaccine for Avian flu. Nor do we have enough of the anti-viral agent Tamiflu to treat more than one percent of our population for the Avian flu. To acquire more anti-viral agent, we would need to get in line behind Britain and France and Canada and others who have tens of millions of doses on order. And where must the factory in Switzerland go to get the raw materials needed to manufacture Tamiflu? To Asia, to the region that will be hit earliest and likely hardest, and, specifically, to China and, right now, only China.

It is true that neither Avian flu nor these other viruses have yet spread geometrically – instantly and irrevocably overcoming health care systems and pulling us backward across thresholds of darkness that we long hoped we would never cross again. And yet this they might do – either entirely on their own in nature or as a result of deliberate human intervention. No intelligence agency, no matter how astute, and no military, no matter how powerful and dedicated, can assure that a few technicians of middling skill using a few thousand dollars worth of readily available equipment in a small and apparently innocuous setting cannot mount a first-order biological attack. It is even possible to synthesize virulent pathogens from scratch, or to engineer and manufacture prions that, introduced undetectedly over time into a nation's food supply, would after a long delay afflict millions with a terrible and often fatal disease. Unfortunately, the permutations are so various that the research establishment as now constituted cannot set up lines of investigation to anticipate even a small proportion of them. Never have we had to fight such a battle, to protect so many people against so many threats that are so silent and so lethal.

But is it reasonable to assume that anyone might resort to biological warfare? Indeed it is. Though Al-Qaida's leadership has been decimated, it has declared that, "We have the right to kill four million Americans – two million of them children [and] it is our right to fight them with chemical and biological weapons." In Al-Istiqlal, the weekly of Islamic Jihad, we read that "it is the duty of Muslims to act in any possible way to acquire weapons of mass destruction, starting with nuclear weapons and ending with chemical and biological weapons." It is hardly necessary, however, to rely solely upon stated intent. One need only weigh the logic of terrorism, its evolution, its absolutist convictions, and the evidence in documents and materials found in terrorist redoubts.

Those who equate terrorism with its targets and take false comfort in attributing to the terrorist the moral status and restraint of his victim should consider that for more than half a century at least eight countries have possessed a collective arsenal of, at times, scores of thousands of nuclear warheads. Still, apart from the first and only use of nuclear weapons, in every trying condition, in crisis and in war, in victory and in defeat, not one has been detonated except in test. Who would gamble that if the terrorist enemy possessed even a single nuclear charge, he would fail to devote all his resources to its detonation in the midst of the maximum number of innocents? And though not as initially dramatic as a nuclear blast, biological warfare is potentially far more destructive than the kind of nuclear attack feasible at the operational level of the terrorist, and biological war is itself distressingly easy to wage.

As the commission on intelligence capabilities reported to the President two months ago: "Biological weapons are cheaper and easier to acquire than nuclear weapons -- and they could be more deadly. The threat is deeply troubling today; it will be more so tomorrow...."

I ask again how it is that we are under prepared either for naturally occurring epidemics of newly emergent diseases or those that are deliberately induced? In comparison to what little we did for decades, we have done much since September 11. But we have far, far, far more to do.

Guided by my duties as a physician and a public official, I propose that we take the measure of this threat and make preparations to engage it with the force and knowledge adequate to throw it back wherever and however it may strike. It need not be invincible and we need not feel defenseless. Means adequate to the success of a defensive plan are present in great profusion. Whereas the approaching biological shift is gathering force like a massing army, providence has massed an army to meet it. Having themselves expanded geometrically, the life sciences have come to the threshold of a great age, and to cross it they need only encouragement and a signal from the body politic to put their resources in play.

We are not without weapons in this war. They are present in the stupendous material and intellectual wealth of the civilized world, which, despite current divisions of action and opinion, has everything to lose in common. They are present in the approximately \$30 trillion combined gross national products of just NATO and Japan. They are present in the great stores of science and technology amassed over thousands of years of civilization; in the many hundreds of universities, advanced research institutions, and hospitals, yes, in the United States and Europe, but also in Latin America, India, China, and dozens of other countries on six continents. They are present in the revolution spawned by information technology and our vast, instant and interconnected ability to communicate and share information. They are present in the private sector's determined focus, which, though frequently condemned for its lack of humanity, could be the instrument that saves us in the end. They are present in the special temperament and brilliance of individual scientists; in the magnificent light that comes of the surprising and ingenious application of new technologies; and in the vigor, intelligence, and decency of free and unoppressed peoples.

I propose an unprecedented effort – a "Manhattan Project for the 21st Century" – not with the goal of creating a destructive new weapon, but to defend against destruction wreaked by infectious disease and biological weapons. I speak of substantial increases in support for fundamental research, medical education, emergency capacity and public health infrastructure; I speak of an unleashing of the private sector and unprecedented collaboration between government and industry and academia; I speak of the creation of secure stores of treatments and vaccines and vast networks of distribution; I speak of action, without excuses, without exceptions; with the goal of protecting every American and the capability to help protect the people of the world.

I call for the creation of the ability to detect, identify, and model any emerging or newly emerging infection, present or future, natural or otherwise; for the ability to engineer the immunization and cure, and to manufacture, distribute, and administer what we need to get it done and to get it done in time. For some years to come, this should be a chief work of the nation, for the good reason that failing to make it so could risk the life of the nation and other nations the world over.

This is a bold vision. But it is the kind of thing that, once accomplished, is done. And it is the kind of thing that calls out to be done, and that, if not done, will indict us forever in the eyes of history. In diverting a portion of our resources to protect nothing less than our lives, the lives of our children, and the life of our civilization, many benefits other than survival would follow in train, not least the satisfaction of having done right. If the process of scientific

discovery proceeds as usually it does, we will come to understand diseases that we do not now understand and find the cures for diseases that we cannot now cure. And, as always, disciplined and decisive action in facing an emergency can, even in the short run, compensate for its costs – by adding to the economy both a potent principle of organization and a stimulus like war but war's opposite in effect. This would power the productive life of the country into new fields, helping transform the information age with unexpected rapidity into the biotechnical age that is to come. All this, if the nation can be properly inspired in its own defense and protection, perhaps just in time.

We have built great cities, dams, and aqueducts. We have built the interstate highway system, bridges, canals, fleets, armies, a world of structures. We have decided upon going to the moon and then done so in a few short years. Can we not, then, build this thing, and take these steps, to protect our lives and the lives of our children, to evade mass death and suffering, that would strike at all classes, all races, all ages? We must open our eyes to face the single greatest threat to our safety and security today, but also to seize our single greatest opportunity.

I am aware of the difficulties. But the United States is as blessed today as it has been since its beginnings. We are the wealthiest, freest, and most scientifically advanced of all societies, the first republican democracy, the first modern state. And although we have suffered criticism of late, we have been willing since our Founding and are willing still to pursue certain ideals. Though not infrequently condemned from the precincts of cynicism, America has mostly left cynics in its wake, sometimes after saving them from floods that they themselves have unleashed.

Today I have tried to impress upon you the urgency I feel in a matter concerning not only America but the world, for pandemics know neither borders, nor race, nor who is rich nor who is poor, they know only what is human, and it is this that they strike, casting aside the vain definitions that otherwise divide us.

It is my pre-eminent obligation as a public servant and my sacred duty as a physician to ask you to support the essence of my proposal. In respect of human mortality, for the sake of your own families and children, for the honor and satisfaction of doing right, I bid you, the stewards of this great institution of higher learning and research, to join me in this essential effort.